Broder, Samuel 1997 B

Dr. Samuel Broder Oral History 1997 B

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National Cancer Institute Oral History Project Interview with Samuel Broder, M.D.

conducted on July 3, 1997, by Gretchen A. Case

at Dr. Broder's office at the IVAX Corporation in Miami, Florida

GC: This is Gretchen Case talking with Samuel Broder in his office at the IVAX Corporation in Miami, Florida. It's July 3rd, 1997, about **11**:00 a.m.

I usually start out by just asking people about your education and what brought you to the National Cancer Institute. What you did before you came and how you ended up there.

SB: Well I went to the University of Michigan for both undergraduate and medical school, and then I went to Stanford University in Palo Alto for training in internal medicine, and then I went to the National Cancer Institute. I arrived at the National Cancer Institute in 1972.

GC: Were you a part of the doctor draft that was going on at the time?

SB: There was a draft, but I was part of the [PHS] Commissioned Corps which was a common way that individuals came to the National Institutes of Health in that era. So I was what was called a clinical associate.

GC: And you came into the Metabolism Branch. Is that right?

SB: Right. That was headed by Dr. Tom Waldmann.

GC: Was Dr. Berlin still around when you came in?

SB: He was around. He was at that point no longer the head of the Metabolism Branch and was pretty much acting as the head of the what is now called the Division of Cancer Biology and Diagnosis, but that was probably not the official name in that era.

GC: So did you mainly work with Dr. Waldmann?

SB: Yes ind eed.

GC: What did you start out doing? Did you come in and set up your own projects?

Were there things that you stepped into the middle of?

SB: No, in that era I pretty much picked up projects that were ongoing. Dr.

Waldmann offered oppprtunities to make modifications or do new projects, but it was pretty much an opportunity to participate in things that were already underway.

GC: Do you remember what you were working on when you first started out there?

SB: Sure. Working on a number of diseases. One disease called common variable hypogammaglobulinemia. Another disease, ataxia telangiectasia. Another disease, Wiskott-Aldrich syndrome. Another disease, intestinal lymphangiectasia. There were a series of important immunologic abnormalities that were being studied in that era.

GC: Were you seeing patients and doing research in the laboratory?

SB: Yes.

GC: So you went on rounds?

SB: Yes.

GC: Can you tell me a little bit about how a typical day would go in the Metabolism Branch?

SB: Well it was what my idea of real clinical investigation should be. There was a component of both clinical activities in what was then called Ward 3-8, and there was a component of laboratory research. And basically the clinical associates were in charge of the patients and followed them every day, did whatever medical procedures were necessary or what other medical care issues might be

necessary. But then also there would be weekly attending rounds where patients were reviewed, progress was followed, ideas were developed, and so on. So it was a good mix of clinical and basic research, and a lot of very interesting things happened on that ward.

The disease ataxia telangiectasia for example in that era was considered a very obscure disease, a component of immunologic abnormalities, mainly of T-cell abnormalities, neurologic abnormalities, and some other pathophysiologic changes. But now it is the center of cancer research, recognizing the problems in DNA repair that are associated with that syndrome. The gene for it has now been cloned and sequenced, and there's a great deal of information now about how the gene works and how abnormalities of that gene may play a role in various forms of cancer, not necessarily related directly to ataxia telangiectasia. So it's a very interesting, very gratifying kind of development.

GC: Now when you were in medical school and when you decided to become a doctor, did you intend to go into cancer research or is this something that you ended up at the National Cancer Institute and developed an interest in oncology there?

SB: I definitely had an interest in cancer for a considerable period of time so that it was not a new development.

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GC: What was it like as a young clinical associate at that time doing research? Can you tell me about what kind of resources you had at your disposal or what the atmosphere in the service or on the branch was lik e?

SB: It was a good atmosphere. It was an atmosphere in which ideas were discussed. The idea of using the patient to guide the research activity to try to tie a clinical observation to a basic science observation is a very gratifying experience. It actually went against what the more official dogma is which is that basic science observations drive clinical research, and in a number of cases it 's really quite the

opposite. Important observations at the bedside or from a clinical perspective can

(drive the kinds of experiments and the kinds of hypotheses that are raised in the laboratory. Or sometimes the persistent and durable commitment to studying the

disease can provide basic research continuity.

Ataxia telangiectasia was a very obscure disease, but then it became very fundamental. And the regulatory mechanisms that are involved and the checkpoint functions of cell cycle regulation as those ideas emerged, the correlation between oncogenes and certain specific translocations of chromosomes all came into play and all linked up with ataxia telangiectasia because it was an ongoing interaction, and that disease became very fundamental

in a lot of the basic research of our era.

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Then it became apparent that there were homologues of the ataxia telangiectasia gene that could be studied in various models, in yeast, in fruit flies, and other systems, and it became an important fundamental focal point for understanding how cells regulate themselves, both in cancer and in other states and just in the physiology of the cell regulation. Because what is now apparent is that there are a number of gateway or checkpoint functions that regulate the so-called G1/S interphase or the G-2/M interphase, and basically the abnormalities in ataxia telangiectasia are very critical. Response to radiation injury or other forms of genotoxic injury can be studied in that model and can be elegantly adapted from

both a human level to yeast to fruit flies and vice versa, all synergizing into

(providing very fundamental information.

Now that we know that it's involved in key aspects of the phosphatidylinositol kinase system, which is very fundamental, even more advances will be made.

But it's a synthesis of very disparate discipline s in one disease entity that would 've been difficult had there not been the continuity and the long-term commitment over decades of studying the patients, and then using the patients to teach what basic research observations might need to be done and then as new basic

research opportunities were open, taking them back to studying the patients in a

very elegant to and fro.

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GC: Was that unique at the time to the NCI, or the NIH, this kind of..... ?

SB: I don't know if it was uniqu e. It was unique in my opinion in terms of its

excellence and its capacity to have the same people move from both a clinical to a laboratory arena and vice versa. But I can't say that it was absolutely unique.

GC: I noted that you moved from the Metabolism Branch over to the Medicine Branch for a year? Is that right?

SB: That's co rrect.

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GC: What was that move all about?

SB: That move was to permit me to essentially become fully certified in oncology from a clinical point of view. So following that period, I was able to become certified by the American Board of Internal Medicine in medical oncology, and I think that added a certain capacity and capabili ty to my abili ty to contribute to the NIH.

GC: And then you came back to the Metabolism Branch after that?

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SB: I came back to the Metabolism Branch for a couple of more years, yes.

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GC: But this time you were a senior investigator.

SB: That's correct.

GC: How is that different than being just a clinical associate?

SB: Well, given the way the Metabolism Branch worked, from outward appearances there actually wouldn't be that much of a difference. From an admini strative point of view there was more work involved and there was management of

budgets and responsibilities and so on, but there was a certain informality and

(lack of attention to hierarchical structure in that branch that I think was unusual.

So I wouldn't say it made no difference but it didn't make as much of a difference as you might think.

GC: This lack of a hierarchy. Was that beneficial in terms of information flow between scientists and between projects?

SB: Yes, I think it was. That kind of a structure requires some unusual components, and I can't say it can always ex ist. It requires certain personality types and a certain type of commonality of purpose and so on. It worked, but it might not

work in every circumstance. It wouldn't work if there was an unusually

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aggressive or greedy personality or something. But in that era, everybody pitched

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in, everybody worked for a common good, and there was no need for an intensely hierarchical structure and the people worked very well without it.

GC: Who else did you work with other than Dr. Waldmann?

SB: I worked with Mike Blaese, I worked with Warren Strober, I worked with Jay Berzofsky, I worked with Dave Nelson, I worked with a number of people.

GC: Would you consult each other on projects or questions that you had?

(**SB:** Sure.

GC: So it sounds like when you came back as a senior investigator, that's when you started taking on administrative responsibilities?

SB: Yes. There were a lot more administrative responsibilities.

GC: And then you took the position of associate director in Clinical Oncology Program (C.O.P.), which sounds lik e it was a lot more administrative.

SB: Yes. In government you can't be sure what a title is. Titles are very misleading.

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You can have a couple of diminutive titles but the person can still be the top

person, or vice versa. An assistant secretary for health, you don't know whether that's a big position or a little position. That position in the C.O.P. meant that I was in charge of the intramural and clinical oncology program, which was made up of several branches and was a very large operation.

GC: Can you tell me about that move? How you came to take that position or how you were selected and what kind of transition that was?

SB: Basically Vince DeVita and Bruce Chabner asked me to do it.

(GC: And that was something you were interested in doing or was it a ... ? Was it an easy decision to move?

SB: It was a complex decision, and it had pros and cons. I was offered more laboratory space to compensate me for doing the move, it meant moving to a different division of the Cancer Institute, and it meant taking on a lot of responsibilities and to be involved in many different issues other than just the science or the clinical end of it. And it required a number of political type interactions, more than, in many cases, the scientific interactions.

GC: What kind of political type interactions?

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SB: Well, whenever you have important branches led by very brilliant people with grant standing and they have competing needs and they have to come to another

office, which would be my office, for resolution, that requires some level of political skill. I'll leave it to others to decide whether I was successful or not.

GC: So what you're really talking about is within the NIH, kind of balancing the needs of different branches.

SB: And the personality and ego needs of the individuals involved.

(**GC:** It must've been interesting.

SB: It was a laugh a minute.

GC: [Laughs] But at the same time you were still conducting your own research. Is that right?

SB: Yes. Shortly after arriving in the new operation, I kept my relationship with the Metabolism Branch and so I didn't actually sever it for a few years.

The Metabolism Branch was a logical referral place for patients with unusual diseases, and it turned out in the very early eighties, I think it was approximately

1981, we saw a case of a young man who had incredible disruption of his immune system who had various types of viral infections, had intestinal lymphoma, had various types of opportunistic infections, and we said to ourselves, "We don't know what this is but we hope we never see it again." It turns out it was the first case of AIDS. One of the first cases of AIDS seen in the Clinical Center and probably one of the first cases seen in the country.

So as that disease suddenly became more important from several points of view, the Department of Health and Human Services itself made it extremely high

priority for people to begin paying attention to it. And basically, one way or

(another, I was asked if I wanted to start paying attention to this new disease and would I do that. So we said, "Yeah, we'll take a look at it in my laboratory." And I did a lot of collaborative work with Robert Gallo's group. And then following his isolation of the virus that causes AIDS, we then made it an effort to try to study new drugs.

I think it's very easy to forget how difficult that period of time was because now we have a lot of effective drugs and people take things for granted. But in that era, there were no drugs that were known to work. Basically people didn't have any ideas of any substantial value, and most of the pharmaceutical industry was not that interested in getting involved or at least didn ' t have dramatically new

ideas. So we made a strong effort, we made a commitment, we found our own internal coll aborations, and it was, in retrospect, a very productive time.

GC: It certainly was. Do you remember what it was that made you look at AZT in particular?

SB: That was part of a collaboration that we were doing with the Burroughs Wellcome Company. Basically, Hironki Mitsuya in my group was able to set up a reasonably reliable assay and then we were able with Bob Yarchoan to move

whatever observations were made in the lab to the clinic. It was ironically at the

(time and even in retrospect an ideal application of what the current Clinical

Center is all about, in that a laboratory element cou ld do certain things and then-not quite as simp ly as I'm about to say-but in effect, take the observation twenty feet down the hall into a clinical area and begin treating patients. And that kind of interaction and that kind of abili ty is really very rare.

In an ironic way, which is still puzzling to me, the NIH has never, as an organization, really "owned" that advantage and that unique attribute. It has de-emphasized that.

GC: Oh really?

SB: Oh yes. Very clearly. The NIH has emphas ized the idea of doing research in AID S, but the NIH has de-emphasized, in my view, inexplicably the phenomenal advantage th at was conferred by a system that was set up maybe at that point thirty or forty years ago beforehand. But it was a perfect antidote to people who might say, "What do you need a Clinical Center for, or why do you need an intramural program?" and all those other things. And here was a classica l example where the intramural program could do what historically the Publ ic Health Serv ice i s sup posed to do, wh ich is to turn science and laboratory technology into an advantage for a public health issue. It' s never been framed

that way in my experience at the NIH, and with time that kind of involvement

(became less and lessimportant and never highlighted. It's a very interesting, almost deliberate omission.

And in part I think it may reflect that the NIH leadership may not actuall y accurately understand what happened, and in part may not recognize the consequences to the country had the Clinical Center not existed or had the kind of freedom that existed in that era and the kind of ability to move from lab to clinic and vice versa not existed.

I think people take a lot of things for granted. For example, the protease inhibitors that everybody talks about are very important advances but they do not work alone. They only work in combination with other agents, and those other

agents predom inant ly we re discovered as part of this process. So this is a kind of progress that people are taking for granted. I think it's import ant to have the historica l record clear because othe rwise you make certain deci sions that have profound effects and may not be the best decision s.

GC: So if th is system of the Clinical Center at the NCI had not been set up, AIDS researc h could've gone a whole different way.

SB: I think so. There's no doubt in my mind. In the last analysis and in the very long

run, you can alw ays argue that things will sort themselves out and that probably is

(true. But I think an enormous amount of time would have been lost, and I think the focal point for maintaining the momentum and the optimism for progress

wou ld have been lost. I think that that aspect of the intramural program is just very, very seldom brought to the table.

GC: That's reall y interestin g because it seems li k e it shou ld be their shinin g star.

SB: We ll , not framed as a shining star kind of issue, I just, I think that . . . . In order to defend and explain to the publi c why one would need a federally funded laboratory-basedcl ini cal reseacr h organization, you have to have clear examples and this is very seldom brought forward. That's all I can say.

GC: Did you get to know your patients very well?

SB: Sure.

GC: And their families?

SB: Sure.

GC: Did you ever have trouble convincing them to work with you on treatments?

(**SB:** Sometimes, but usually patients that had made the process of being referred to the Clinical Center already were highly motivated patients and had already made a decision that they wanted sort of an experimental drug, that they didn't want to just sit home or do whatever. So they made a decision. They preselected themselves.

GC: You came in as director in 1988.

SB: Eighty-nine, I believe. I think I was sworn in in '89. The announcement might've been made in '88.

GC: Okay. Some of these things get a little fuzzy-

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SB: No, I was swo rn in in January of '89.

GC: Okay. I'm so rry abo ut that. H ow did you rise to the attention of the people selecting the director?

SB: Don't know. [Laughter]

GC: Who call ed you and told you you were being selected or being consider ed ? Do yo u r e memb e r anything about that process?

(**SB:** I got a call from the White House, one of the staffers for the White House, and also a call from probably someb ody at the D epart ment of H ealt h and Human Services.

GC: Were you surp rised? What was your reaction?

SB: Well, I wouldn't say I was surpri sed but I think that I was ambi valent.

GC: Really.

SB: Tru e.

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GC: Why is that?

SB: In that era, the NIH, for better or for worse, was not necessarily viewed with the same degree of importance within the chain of authority of the administration as it h as now become. And I think that there were many, many other agendas at work in that era that may or may not be quite as obvious in the scientific world now.

There were many issues related to what I consider non-scientific policy issues. People have forgotten, there used to be a gag rule for various issues. Th ere was a certain political agenda that was not necessarily the kind of political agenda that

people now have evolved to. And I think in taking the job of being the head of

(the NCI, the most important function in my view would be to serve as an emissary of the importance of the NIH and the NCI, and as, for want of a better

term, a guardian against a diversion of the NIH 's mission and its apolitical quality.

I think those are attributes that, again, people kind of take for granted or can' t believe are relevant because times have changed. But there was a different era in the late eighties than there might be now. And I think there was an imp ortant need to make sure that the NIH was protected and was served w ith the kind of academic independence and freedom that everybody expects it to have. And so from my point of view, a very important function would be, for whoever took the job, to defend that.

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For example, at least as far as I can tell within the NCI, we never permitted a Schedule C appointment, even though there was enormous pressure to do that. Schedule C appointments, for those that are not aficionados, is a political appointment, "here's my friend, give him a job," kind of thing. That's the political spoils of war, so to speak. Most agencies of government have a certain number of those kind of appointments. We never permitted that, at least as far as I could control events during my entire tenure. And there was a lot of pressure, particularly in an earlier phase for that to happen.

So I think that those are the simple things lik e that that may not be at the front of

(everybody's agenda, but those kind of very simple fundamental things were important to defend in that era. I had to decide is that what I really wanted to do.

So those were the issues.

GC: Was there something that finally tipped your decision?

SB: Well, what tipped the decision was that I felt I had a responsibility if that was something that was possible, and that I felt I was probably in a better position to do things that I outlined than other candidates. I thought I shou ld do it and I did. I was very particularly worried about a weak leader, or a politically influenced leader in that era because I felt it could have very dramatic effects in the long term. So the independenceof the Institute was very important and the

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independence of the NIH process. And I think NIH is very independent, but it's not an independence that can be taken for granted.

GC: Once you decided to be director, did you come in with goals? Certain programs you wanted to push forward or certain initiatives you were ready to take?

SB: Yes. The primary set of goals that I wanted to take care of were one, to make sure that we had effective training and medical curricula in medical schools, particularly that would provide new avenues for cancer research and the training and development of clinical researchers who understood oncology from a prevention, diagnosis, and treatment point of view. Not just treatment, but across the board. And I was very interested in curriculum reform in medical schools, and in fact we expanded so-call ed R-25 grants that went to medical schoo ls to help their curriculum formation, and I thought that was an important goal.

I thought that keeping a balance among the components of the institute, which would be essentiall y a commitment to basic research, which always is the most fundam ental commitment that the NCI can make, to make sure our clinical trials apparatus in prevention and treatment were strong and had high integrity and effectiveness, and to make sure the cancer centers program, which is not unique

but is speci al to the Cancer Institute, was allowed to flourish.

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Within that context, I thought it was important to allow the cancer centers concept to be adapted around specific diseases, particularly diseases where we hadn't apparently made a lot of progress. What I was observing is that that was a sort of self-fulfilling kind of prophecy where people would say, "Well, you haven't made much progress in prostate cancer, therefore don't put any money into it." And analogously for other diseases. So we set up a specialized program of research excellence in lung, breast cancer, and prostate cancer, the major killers of men and women in this country, to allow independence and freedom of action and interdisciplinary research and I think that program has worked out very nicely.

Then last, but certainly not least, I thought it was very important for the Institute to address from a scientific perspective the vast disparities that existed in some of the populations in the country. The African-American community in some diseases actually, for some forms of cancer, displays an increasing death rate, while in the general population, the death rate is falling for certain cancer types, and that was completely unacceptable. So we set up programs to deal with disproportionate burden of cancer and particularly to try to deal with issues such as cancer and poverty, which I don't believe received as much attention as it should, because there are special issues related to those relationships and we made a strong commitment to that.

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We also developed a science enrichment program which, at least w hi le it lasted, was very effective. The goal was to bring individual students from impoverished backgrounds and inner cities and impoverished rural arenas and bring them into a science-enriching experience. If they had excellence of background in science and commitment and so on, then we didn't want some external barrier to block them. We had a program at Frederick, and then eventuall y made it an extramural program. I think that was an interesting experiment. I don't even know if it's stil l being continued.

GC: I think it is. I think it may have changed a little bit but I have read a littl e bit

(about it lately. I think there's still something going on.

SB: But the concept of taking teenagers in their second or third year of high school and bringing them in for what amounts to a high school academy of science to show them opportunities and to prove to them that they have a number of

oppo rtunities to open up vistas that might not be available. I think that was all a

very interesting and productive opportunity, and I'm glad I had the chance to be part of it.

GC: What was going on in Frederick at the time that you were director? How big was

that program?

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.SB: It was a very large program, the major commitment to biological response modifiers and there were other support services being done.

GC: Did you go out there as part of your duties?

SB: I made periodic visits, but I wouldn't say that I went there frequently. I went there several times a year, but not weekly.

GC: Okay. What was a typical day like as the Director?

(**SB:** A typical day would be responding to major issues of the day, preparing for congressional testimony, preparing for advisory committees, trying to set priorities, especially budget priorities, mediating disputes, things like that.

GC: Were you still connected to your lab?

SB: I was connected, but with time, an ever-diminishing connection. I personally don't believe that one can credibly be the director of the NCI and maintain a major laboratory effort. It is my own personal view, and maybe it can be adapted to some exceptions. I think certainly a lab involvement is possible, but to assume a meaningful leadership role of a significant laboratory at the same time that

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you're running the NCI means that one or the other is going to suffer, and it means that you're really not doing both jobs. That's my personal view.

Now you may say that you're doing the one or the other, but I personally think that the head of the NCI is more than a full-time job, and running most laboratories is more than a full-time job. So if you say you're running a laboratory, what you really mean is that you must have somebody there who's really running it and you come periodically and ceremonially and do things.

Now there can be some exceptions to that, as there are to every rule, but I just

(think that it is very difficult to really run a laboratory in the way that term is usually used. In the sense that if something goes wrong with the lab, you are

prepared to say, "I am responsible." Not "I'm too busy being the NCI director and I wasn't able to monitor this." With that kind of a caveat, I think it's very difficult to do both.

GC: Who did you work with on a daily basis as director?

SB: I worked with the deputy, I worked with the budget office, I worked with an assortment of division directors, I worked with various scientists, I worked with visiting scientists and professors and people who were in various Fogarty

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programs and so on. It was a pretty full day. I usually didn't get home till about eight.

GC: Starting at about seven or eight?

SB: No, I didn't start that early, but startin g at about eight-thirty or nine, didn't get home ti11 eight.

GC: A long day.

(**SB:** It was a long day. Plus half-days on Saturday. I'm working much lessnow than I did in the government.

GC: Who was your deputy director?

SB: Ed Sondik before my retirement, and Dan Ihde, and at the beginning I had Maryann Roper. There were a number of segments when there was no deputy and there would have to be an acting deputy.

GC: You were in office as director as the administration changed. How did that

change your position or did it, I guess I should ask.

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SB: I think it did change the position very much in that I had developed a working relationship with most of the people in the Reagan and Bush administrations, and I think especially toward the very end had established what I intended to accomplish which was the independence of the NIH and the NCI intramural program and a certain very strong measure of respect. And a practical operational line of communication especially with Lou Su ll i van and others.

I think that on balance when there was a change of administration, particularly when Dr. [Bernadine] Healy was asked to leave, there was a very strong gap and

it wasn't clear who I was reporting to, or who required the kind of

(communicaiton that you need to do in this setting.

Then at least for a six-month period of time or longer, it got political in a negative way, in a way that I had been trying to avoid, not through anybody's fault, but because there was no coordinated structure. Dr. Varmus had not yet arrived, and so it meant that individua ls from anywhere in the administration, not even connected to NIH, could sudden ly call you up and want you to do something and wanted you to do this and why don't you fund this and whatever. I believe that we established a very clear set of understandings in the prior administration that you don't do that. You don't call us up to ask you to fund somebody in such a district and so on.

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I think there was a certain interim of time where those lines of communication weren't clear and I think it finally did get straightened out, but at the beginning it was very chaotic. And it caused unnecessary stress because who wants to continuously remind people that no, that's not how we do it. If you have a proposal, you have to send it in for peer review. No, I'm not going to just fund the study, send money to somebody X, Y, or Z or whatever. That's not how we do it. So eventually it got straightened out, but there was a six-month period of time where it got pretty chaotic.

GC: And once it got straightened out, was it different than it had been with the

(previous administration?

SB: At that point I wasn't around long enough to do a comparison. I can't give you a comparator, so I can't really tell you. I don't have enough of a sample size.

GC: Okay. What are you proudest of? I'll ask the question two ways or maybe it 's two different answers. What are you proudest of during your time at the NCI or another way I sometimes ask it is where did you have the most fun? What did you enjoy the most?

SB: You mean during my entire time at NCI or as director?

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GC: During your entire time, but then we can ask the question again just as director because-

SB: During my entire time, the most fun thing was to be able to refute the destructive pessimism that passed for a wise sagacious advice that AIDS was untreatable.

And again that's an area where people quickly forget, but there were very prestigious and important policymakers who felt that intervention against AIDS and the virus which causes it was inherently impossible and that it was a waste of money and that the only hope was to begin a fifteen- or twenty-year basic

research program without any real attempt to adapt what might be doable.

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I feel very happy about the role that my life played in helping to refute that prophecy, which perhaps no one remembersbut if you actually were to pull, in Nexis whatever the citations were in that era, you wou ld see article after article about AIDS will be untreatable, National Academy of Science forum says AIDS untreatable, don't waste money on treatment, all the different things that

people said in that era. And I think that was very gratifying and being able to use a laboratory-based effort to give people hope is a very unusual thing. It happens

to most people never. In my situation, at least, it happened during my mid- career. So many scienti sts don ' t have that experience, never have that

opportunity. Not through any fault of their own, it's just a matter of what hand

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you have to play. But this was my hand. My laboratory was able to make the contribution and that makes me feel very positive.

In terms *of* the things within the NCI, I think by and large we gave people fair administration of the science po rtfo lio and we made a commitment for the integrity of that portfolio. And we made a strong effort to make sure the public could respect and appreciate and not have fear from any aspects *of* the research agenda that we had. That they could feel assured that their tax dollars were going for a cure for cancer. I think that's the part I feel very positive about.

(**GC:** Was there anything that stands out in your years as director speci fica ll y ?

SB: No, I think it's all a blend. When you're in an administrative job, there's usually not one thing. It' s usually a contin uity of a lot of different things. In a laboratory context, it can be one major discovery, a eureka phenomenon, but in an administrative role it's usually not that way. I believe that as a practical matter, in fiscal year '92 the NCI received the largest dollar increases that it ever had gotten for its budget in the history of the Institute. Not necessarily as a percentage, but as a dollar amount, and I think that makes me feel good. That base increase was very positive.

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'GC: Now you sent me an article last fall that called you the champion or a champion of cancer education. Could you tell me about your interestsin cancer education?

[End Side A, Tape 1]

[Begin Side B, Tape 1]

SB: Well that's what I was talking about curriculum reform and the aspect of curricu la at medical schools or related professional schools. I think the part of the Institute

that received a bit too much neglect over the years was the area that had dealt

(with cancer education of medical students or related health-care professionals. I

saw that as a loss of an opportunity because you cou ld set a certain agenda, you cou ld set a certain mindset, you could set a certain philosophy in place that would last a lif etim e, if you had the right curricula and if you had the right kind of commitment. And I could see that we were losing that and many leaderspaid almost no attention to that.

That aspect of the In stitute was supposed to happ en through a black box, and I felt very strong ly that it was important to try to reach young professionals particularly medical students, but others as well, to get them interested in

prevention, to get them interested in the public health aspects of cancer, to get

I them interestedin environmental research as a scient ifi c undertaking as opposed

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to a political undertaking, to get them interested in the research method and science and the scientific method and all those things. And for a very small expenditure of money, we could accomplish that, so I was very happy that we were able to do that. Although that program is probably now being de-emphasized, you capture somebody for fifty years when you do that. It's a pretty good investment.

GC: Another issue that's come up a lot in the history of the NCI is the idea of funding research or arranging research through contracts versus grants. Is that an issue

that came up while you were a director?

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SB: It's a perennial issue, and in one era I think it had a great deal of merit. In other words, the concern over that issue was acute and on the mark because there may have been too little attention to the importance of protecting investigator-initiated research and avoiding entanglements in which the contract mechanism was being used to further the academic career activities of a full-time government employee, or related issues.

So the importance to separate that and to give as much attention as possible to grants in aid or research project grants which have a crucial element of independence-it's an assistance mechanism as opposed to a pay-for-performance mechanism, which a contract is-that those kinds of differences were very

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important to preserve. And I think that we've always tried to be sensiti ve to that. In fact the contract line continued to fall during my administration, and we certainly diminished the use of contracts as much as we could.

But having said that, I think that debate at this point has become artifici al and strain ed and often has the element of a straw man kind of approach where people are ritualistically discussing the pros and cons of research project grant versus

cont racts. Well, really, if they're properly administered and there's a sensiti v ity to what each has to do, they're both important mechanisms. I think it's more

important to talk about the substance of what needs to be done and how to

(prevent and cure the diseases we're dealing with and recognizing the safeguards that you need to have, but I think there's probably too much attention to that in

the modern era.

GC: That's an interesting viewpoint. Another big issue has always been advocacy groups or people outside the NCI, their involvementin the NCl's research. Was that an issue during the time you were either a researcher or as director?

SB: It was an issue, but not only at the time I was the director. There was a strong set of related issues w ith AID S and AIDS activism, and cancer and cancer activism. I think patient advocacy is very important. I think, in fact, the categorical institute concept, which has served the NIH very well, in part derives from patient

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advocacy. In a certain sense, it ' s an acknowledgment of the importance of the NIH system that patients feel they need to be involved. And secondly, certain patient groups do not feel affirmed unless they have an institute that represents the disease that they're advocating for. And I think that that's, in a way, a very positive statement of the importance of the programs, and the relevance of the programs.

Thus, patient advocacy is important, and it plays an important role in the NIH process. The reality, unfortunately, is that patient advocacy cannot change the

science in certain ways, and in the political process it can sometimes remove

(admini strative barriers, it can sometimes remove apathy and inertia, it can be a force for accountability, but very rarely can patient advocacy stimu late scientific advance. That process goes by a different route.

So I think that what patients and patient advocacy can do is address issues whe n there is dramatic disproportionality of funding in a certain field. They can correct such a problem or they can help advocate for a correction. If there is a set of regulations that impair clinical research or clinical trials, they can change things for the better.

If there is demagogical intervention from a congressional committee or from a congressman or a senator that turns out to be destructive to the integrity of

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science, sometimes patient advocacy is the only antidote to that because scientists by and large are relatively defenseless. That kind of a process occasionally can self-ignite and can cause significant problems by destructive people. And as an individual scientist or science administrator, there's not much that one can do to stop that, but an alert and vigilant patient advocacy organization can write a letter or call up a particular congressman or senator and say, "You may think you're doing a nice job bashing the NIH or trashing this or trashing that, but you're really being very destructive and we want you to stop."

That can be highly effective and probably is done too litt le by patient advocacy

(groups. But when it <u>is</u> done it can actually be very effective, because in the last analysis most patient advocacy groups need to have an independent and humanistic and committed NIH, and you can't have that when there's destructive political forces around.

So patient advocacy certain ly has a lot of important roles, but what patient advocacy cannot do is create a scientific advance. And when one takes two steps back and realizes that, recognizing there may be an occasional exception, but recognizing that that is just generally the way it works, you have to pause a little bit.

I also think there are occasional times when patient advocacy can be self- defeating and that it doesn't acknowledge the kinds of personalities and temperament that essentially inform who becomesa scientist or technology- oriented person to begin with. Many scientists and clinical researchers go into the field because they have the personality makeup, as well as the intellectual and technical background, and most scientists believe in the scientific method, believe in discussion and logic, in very quiet, tempered debate; in a debate that is informed by ideas and with a heavy reliance on the written word and with a de- emphasis on emotionality or unnecessary demonstrativeness in the process of

having a dialogue. And they can be influenced to avoid fields where those kind

(of conditions don't prevail, or when they won't be protected in those kind of fields.

I think that's just a reality. So that if a particular scientist has a choice of going to study field X versus field Y, and field X might over-stress them periodically or force them into a situation where they might have more negative interaction with advocacy groups than they might want, they'll go to Y. I've never heard that outwardly stated by anybody, but it is true in my opinion, that you can negatively influence who goes into a field, and that the advocacy groups may not always recognize that there are people at the other end of their advocacy. And I think that's just the reality.

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GC: I'm sur e that never occurs to them that they're having that kind of effect.

SB: Well, that they may have that effect.

GC: Did you ever personally have a situati on where ... you talked about that an advocacy group could be very useful in changing the way someone in a political position is affecting the scienti st's research. Did you ever personally have that kind of experience where-

SB: Well, I'd better not go further than I've gone. I think I'm speaking in the general (context. I don't want to get into any more speci fics than that.

GC: Okay. Mary Lasker is someone who was always a big friend to the NCI. Is she someone you ever had contact with or did you know her?

SB: Yes indeed. I had a lot of contact with her, presumably most of it before she died-

[Laughter]

SB:

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-but I had a lot of contact with her. She was a very wonderful woman. A very elegant, committ ed woman. She was the prototype of all advocacy groups and

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was single-handedly the most effective advocacy person in the history of science. She was a very excell ent person. Very smart, very gifted. So I think sh was essentiall y the pioneer of patient advocacy and is, as I say, in my opin ion the most effective patient or citizen advocate in the history of sci en ce.

She ' s responsible in large measure for the strength and vitality of the current categorical institute system. That's a system in which one can humaniz and particulari ze the scientific method so that the public is making a commi{ment to all eviating specifi c diseases and, therefore, can respond, as opposed to do in g something whic h sounds imp ortant, but might be a little bit more amoq?hous such as supporting science in the abstract. People might or might not be as

enth usiastic to support abstractions. So if you ask a taxpayer would theo/ be

w i l lin g to support cancer cures, they might say yes. If it's just, can we 9upport the National Institutes of Health, the answer might be no. And I think that oncept is not a trivial one.

But I think that what she establi shed was a system in which you cannot help the NIH as an entity without helping each of the categorical institutes, and you cannot help the categorical institutes without helping the NIH and you cannot

help <u>any</u> given categorical institute without helping fill categorical instiWtes. I

think that that's on balance. It may not appear that way in any given y ar, but

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over time that' s the way it works. And I think that quite frankly that system may or may not be apparent to outside observers.

GC: You think she was responsible for that.

SB: I think she was responsible for that. I mean the seeds of it were there before she came along, but I think she definitely strengthened that concept. And she had a very innocent but persistent view that you could solve problems, and in that sense brought a clarity that sometimes is necessary in a comp li cated arena. Somet ime s

it ' s necessary for an outsider to come in and clarify something and simplify it a

(little bit because ind iv idu al scientists focusing on the enormous complexity of what they were dealing with might not really maintain the focus and the

simp lici ty of the message.

But she understood, at least intuitively, the concept that I've just given you. And that concept is not just a fiscal concept: you cannot help the NIH without helping all the institutes, and you can't help the institutes without helping the NIH, and

.you can't help any one institute w it hout helping all institutes. That's true scientifica ll y as wel l as from a financial or resource a, llocation point of view.

In the early seventies, there was a very strong commitment given to the NCI and

l creating the National Cancer Program. What that did, in part, is help fuel the

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molecular revolution. One could say it had the molecular revolution that we now know and see every day in astonishing things that have resulted from the idea of recombinant DNA technology. Is that something that would 've happened anyway? Probably. But the NCI and the allocation of resources in the context of cancer research fueled that revolution. Fueled many of the applications of recombinant DNA technology, expanded concepts such as oncogenes and suppressor genes and the concept of checkpoint function and cell regulation and DNA repair and all the different issues that now everybody talks about on a routine basis.

(But what has emerged, as anyone could have anticipated at the time, is that it's impossible to make a scientific advance in cancer without making a scientific advance in every disease and in science generally. Oncogenes from a physiologic point of view don't just function in cancer. Adhesion molecules, which are incredibly important for understanding the process of metastasis, don't just function in metastatic disease but have all sorts of relationships in a range of

diseases, including inflammatory diseases, asthma, you name it. The concept of applying the technologies of cloning and sequencing genes is applied to everything.

In a sense, the early funding of the NCI, the National Cancer Program in the early

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seventies, laid the groundwork for the Human Genome Project. And I think that

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element is an inconvenient fact and is an ignored fact. So I think many people don't recognize that.

GC: I think you're right. You were still in medical school then when the Cancer Act was passed. Is that correct?

SB: No. I was a resident at that point.

GC: Did you realize at that time the import of this occasion?

(**SB:** No. Why should I? Most people who live in the real world, which is outside the beltway, wouldn't realize the implications of a very esoteric act li ke that. A very esoteric program from that point of view. There are a lot of things that happen at

the NIH, which the average public doesn't understand in detail but feels the effects of. That's why it's very important to have core philosophies and to enunciate your core philosophies.

I think Dr. Healy did a good job. I think many people didn't agree with her on many occasions, but I think she understood and she grasped the importance of enunciating this philosophy clearly and specifically and to the public, not to other scientists, not to people inside the beltway, not to lobbyists, not to staffers and Congress, but to the public. I think that' s an important goal, probably among the

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most im portant functions of the office of the director of NIH, and indirectly an important function, maybe not quite as important, for the head of the Cancer Institute.

GC: Another program, the Special Virus Cancer Program, was around for a long time and the way it's been explained to me is that it never really ended, it changed very drasticall y. Can you tell me-

SB: Like dinosaurs evolved into birds.

(**GC:** Where was it when you became director?

SB: Where was it when I became director? It was an atavar that people still l ik e to fight about. The Speci al Viral Cancer Program was another example that people argue was a failur e. Well, it was not a failure. It most dramatically was not a failure. It laid the groundwork and the basis for under standing AIDS and for beginning therapeutic interventions against AIDS.

It 's high ly inappropriate in my view to argue that, no that doesn't count, and that you can't cite how a commitment to certain aspects of cancer research can have applications in another important disease arena, and that doesn't count. At the same time, the person who is doing the "discounting" wo uld lik ely be arguing that

one needs to have a more ecumenical outlook and one needs to avoid categorical institutes and so on. Often those two go togeth er.

I don 't know why, but usually people who critique or diminish certain accomplishments of the National Cancer Program will, in thesame context, diminish the whole categorical institute concept. And I don 't know why those two are linked but it's been my anecdotal experience that they usually are.

People who recite a certain aspect of the Cancer lnstitute 's actions, as part of the National Cancer Program, as a failure will then simu lt aneousl y also argue for a

diminution of the categorical institute concept. The two are contradictory, but

nobody ever points it out.

If you are an ecumenist and you believe that science and facts cannot be placed into a rigid box or a specific little cubbyhole, that's fine and it's true, but then one also has to recognize areas where a commitment to a categorical research concept productively yielded knowledge, and important knowledge, in another arena.

So this special viral cancer program, in fact, did lead to critical information about the relationship between viruses and cancer; for example Bob Gallo's discovery of HTLV-1 as a cause of adult T-cell leukemia, and it did help in understanding a

future disease (AIDS), at that point still not known. And at a minimum, it allows

you to say it has made dramatic understandings in the relationship between

cancer and immunodeficiency disease, wh ich is a very important topic in its own right.

But in a more practical sense, the identification by Temin and Baltimore and others that there was an enzyme called reverse transcript aseallowed a specific molecular target and allowed rational targeting for therapeutic intervention against retroviruses and then an understanding of where to begin when one focused on the AIDS epidemic.

In that special sense, the viral cancer program was a dramatic success and all you

have to do is ask, "What if it hadn't happened? What if it hadn't taken place?

What if that funding hadn't been there?" You can alw ays argue, well of course, it still would have gone on anyway. I don't think that's a fair argument, and it is not likely to be true.

I think very few people, probably no one in a policymaking, decision-making mode at the NIH level, really knows that AZT was ini tial ly synthesized by Jerome Horwitz under a grant from the NCI. It was not orig in ally synthesized by Burroughs Wellcome. It's a fact. And it' s true that the drug was initially synthesized for the purposes of cancer research. Jerome Horwitz was at what was then called the Detroit Institute for Cancer Research, now called the Michigan Cancer Foundation.

I think we need to make sure that we understand the historical issues here and that we ask the question, "What is the best way to advance science in the real world and in the way things are really done using taxpayer money?" In my opinion, the NIH has either intentionally or accidentally evolved a very excellent way of doing it. It's called the categorical institute concept where all institutes work togethe,r but all institutes work individually and where you get a scientific cross-fertilization from one institute to another, then both institutes and NIH get credit.

So I think there have been phenomenal offshoots from the National Cancer

(Program efforts in immunology, infectious disease, and neurology. There's a whole realm of cross-fertilization. I really have my doubts if in the real world

recognizing the resources that are necessary and the political process that is necessary to generate those resources, that those kinds of commitments would've been made without consolidating around a National Cancer Program.

GC: Along those lines of inter-institute work, did you ever have contact with directors of the other institutes while you were the director?

SB: Yes. I had a lot.

GC: What kind of contact would that be?

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SB: Scientific, administrative, a lot of contact.

GC: What prompted your decision to leave the Institute ?

SB: I didn't want to work there anymore.

[Laughter]

SB: I think it's very important in a position, especially a presidential appointment, not to become a "lifer." The NCI is probably the only career presidential appointment

(in the department. I may be wrong on that, but if I'm wrong, I'm not wrong by much. While it's not a political, Senate-confirmed appointment, it is a presidential appointment. And my view is that all presidential appointment-type

positions or their equivalent, civil service or senior executive service positions at a high rank, require some kind of self-impos ed term limit.

I don't think it's true in all cases. I think there can be exceptions, and I think that there are certainly some exceptions at the NIH that are perfectly appropriate, but I think by and large, for the most part, if you're going to be heading a multi -bill ion- dollar operation, it is better for all parties to have a self-imp osed term limit. And I

think there are several reasons.

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One, anybody who serves in that role should have a very focused agenda of what he or she wants to accomplish, and should not view it as just, I've got all the time in the world, I've got a whole lifetime ahead of me. Because with that attitude, you really won't get things done. It requires a certain degree of commitment to get certain things done.

Second, the individual should have some sort of statement of pr in cip les that he or she wants to defend-some core set of principles and wi ll set a tone for that. You cannot set principles, particularly in certain arenas, without using up your

welcome in Washington, and there's no way of getting around it. And so I think

(that's a reality.

But then if your goal is to stay beyond a certain point, then you have to become politically adroit, then you have to start learning how to be a political in-fighter, then you have to know when to give and when to hold. The degree of compromises you might need to do beyond a certain amount of time become too large to maintain the core principles. So if your principles are the absolut e independence of scientists, the independence of grantees, the independence of the scientific method, the apolitical nature of the NIH, the need to have zero tolerance for fraud and waste and abuse, the need to maintain high standards in

the stewardship of government-funded grants, those things, the need to be fair and to avoid abuses of the scientific misconduct investigatory process, to protect

scientists from unfair witch-hunting, but at the same time, to act decisively in protection of the public good, you can't stay forever. If you believe that these are all principles you have to defend, then there's only a fixed time limit that you can do them.

Because sooner or later, if you don't have a fixed time limit, then you have to have other people do your work, and you have to start becoming a kind of political impresario and you have to develop skills, or exercise skills that are more suited to other agencies of government. The NIH should not be a harbor for

political cuteness or classical inside-the-beltway political maneuvering. It's not

(just another agency. It is the premiere agency of the government.

So in order to hold a high-ranking position and to do it in the way that you need to do it, I don't see any alternative to having a self-imposed term limit. And it's also important to avoid a problem where because you've been in office so long or held a particular office, you get confused between yourself and what the agency mission is because after a certain amount of time, you can win every fight by virtue of your authority, you think you're always right and I think that has a negative effect in managing things. I think, in particular, in the scientific method, I think it's important to have an infusion of new ideas and so on and to have

people take a fresh look at things.

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Beyond a certain amount of time, you may find that you're suddenly spending a lot of time defending what you did earlier in your career and proving yourself right as opposed to being open to a real second look.

So I think all of those things require, in my view, a presupposition that time in office will be self-imposed and limited. I think you can always argue, "Should it be five years? Should it be six years?" And six years was about the right time for me.

GC: Did you know that going into the position?

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SB: Yes. I wasn't sure exactly what the time limit shou ld be, but it was very clear to me that you should not approach a high-ranking position like that as a for-life tenureship. There are a lot of positions in the government that are lik e that. The term of the commissioner of the FDA, for example, shouldn't be so short that you can't get anything done, but it should not be a very long tenure, either. There are a lot of positions like that. And I think it's very important to have that kind of philosophy.

GC: You talked about completing your agenda, were you satisfied with what you'd

done during your time?

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SB: Yes. I believe that for the things that I did, I played the hand that was dealt to me, in the way that established the principles and defended the principles that the Institute needed. They were not always the most popular decisions, but I believe even in retrospect that they were the correct ones. Most of the decisions in one sense were easy to make because they followed very simple principles of what you have to do to be the steward of the public's money and what you have to do where people are expecting a high level of professionalism and a high level of

care in their behalf. So that element of it I feel very positive about.

GC: In terms of the goals we talked about that you set for yourse lf, did you feel like (you accomplished those goals on cancer education and-?

SB: Yes. Cancer education programs increased, the cancer center's program became stronger than ever, a new subsidiary of the cancer center's program, specialized programs in research excellence or programs were implemented. We developed a science enrichment program. We developed probably the greatest emphasis that the Institute ever made on the relationship between cancer and poverty, including funding instruments specifically to address that. We made it a very high priority, a policy at the Institute to address the disproportionate death rate in

African-Americans versus genera l population.

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We made very strong commitments to training, we defended basic science and the peer review system and especi ally made a very strong effort to announce that we will protect the peer review system from politics. We tried to develop flexibility and to protect certain types of creative processes so that that part of the Institute was very strong. We tried to develop a sensitivity for investigators whose funding might be on the borderline and who had interesting ideas but who still couldn't convince peer review groups that they were worth taking a chance. So we developed small grants programs and on occasion a flexible program for giving people a chance to establish their pilot results through various mechanisms

including supplements to core grants, and so on.

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All of those things make me feel very positive and affirm that it was a good experience and I'm very glad to have done it.

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SB:

GC:

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Were there any major setbacks? I'm sure there were setbacks. Do any stand out or any goals that just didn't pan out?

No. I achieved the goals I set for myself.

That's great. Well, I'm wrapping up my questions now. One thing I always like to ask people is, with whom else should I speak? I' m trying to get a broad sense of-

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SB: I don't know what your objective is.

GC: My objective is to collect as much as I can of the words of the people who made the history of the NCI. I'm looking at people from-

SB: Is it lik e a Depression -era oral history project?

[Laughter]

GC: Yes, something lik e that. Trying to get voices from all levels from all areas of the

(NCI and as I interview each person, I ask who else do you think would add to the record?

SB: I think that other than the obvious other Institute directors, I'm not sure that I can give you anyone who would add specifica lly to the programs. Maryann Roper was my deputy, Dan Ihde was my deputy, he might be a very good person to talk to about some of the clinical issues, he was a superb clinician.

GC: Anybody from the Metabolism Branch?

SB: Tom Waldmann would be a very excellent person to talk to.

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GC: Clinical Center?

SB: Unfortunately probably the best person to talk to is now decease,dMort Lipsett.

But John Gallin would be very good. He's very good. Okay?

GC: Okay. Have I missed anything that you'd like to add to the record?

SB: No. You did good.

GC: Great. Thank you.

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[End of interview]

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